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IN THE UNITED STATES PATENT OFFICE

Appln serial No. 10/083,529

Applicant: U.N. Das

Title: a method of stabilizing and potentiating....

Docket No UND 99.02 D 1

Primary Exr: Alton Pryor

Group Art Unit 1616

**Response to the Office Action mailed 9/30/2005**

The following documents are enclosed with this response:

1. A substitute specification as directed by the Examiner, without the single figure;
2. A copy of the amended claims showing deletions and additions;
3. A clean copy of the claims as amended in this response: and,
4. Exhibit A, comprising photocopies of original text pages 18,19,31,36 and 45, to assist the examiner.

**Please amend the claims on file as seen in the attached copy of the amended claims showing deletions and additions.**

**Substitute specification:** The terms Angiostatin and Endostatin in the substitute specification are capitalized as directed, and acknowledged as trademarks once. The paragraphs are numbered in the substitute specification as suggested by the examiner. The medical and pharmaceutical terms in the text are retained and are submitted as intelligible in the context of the invention, in light of the terminology in several references listed by the inventor at the end of the text. Favorable consideration of this matter is requested.

It is submitted that the text in the substitute specification is re-formatted correcting typographical and grammar errors, without adding any substance.

**Claim Rejections:** The Examiner is thanked for allowing subject matter in claims 5-7.

35 USC 112 rejection of claim 7: Claim 7 has been rejected based on the recitation that the anti-angiogenic substance is co-valently linked to the fatty acid.

It is submitted that in page 31 of the text as originally filed, there is a supporting statement that the anti-angiogenic substance is co-valently linked to the fatty acid. It is also submitted that co-valent linking is a term known in the art. Notwithstanding, the amended claim 7 now presented recites that the anti-angiogenic substance is **coupled** with the polyunsaturated fatty acid, which is supported on page 18 of the text as originally filed. Coupling or co-valent linking is equivalent of “mixing” as already recited in claim 7 as originally filed. It is believed therefore that the 35 USC 112 rejection of claim 7 is overcome.

35 USC rejection of claims 1 and 3:

Claim 1 has been rejected as obvious over a combination of Yanai and Kokura: The inventor is aware, as evidenced by the prior-art discussion in the text, of the administration of an anti-angiogenic substance and a fatty acid separately for treating tumors. The present invention, as now recited in the amended claim 1 is directed to a method involving intra-arterially injecting a salt solution mixture of a polyunsaturated fatty acid and an anti-angiogenic substance. It is noted that the original text, at least on page 31 states regarding “mixture” and also “salt solution”.

The inventor has discovered in his experiments and medical practice that anti-angiogenic substances (which are intrinsically unstable) are stabilized and potentiated in their action by the addition of selective fatty acids used in a salt solution mixture with a suitable salt such as lithium. The inventor has successfully treated giant tumor cell of bone and hepatocellular carcinoma with a salt solution mixture of an anti-angiogenic substance and a fatty acid. The salt could be lithium, or sodium or potassium (see paragraph on Equivalents on the original text page 45), for example, as supported by the text as originally filed. The Examiner’s kind attention is drawn to the statement on the original page 19, to “salts such as lithium”.

The Examiner’s attention is also drawn to the passage on page 36 as originally filed, wherein is stated, “More particularly, it is realized through this invention that by delivering a chosen mixture of salts of predetermined polyunsaturated fatty acids and predetermined anti-angiogenic substance(s) to the tumor site.....a very beneficial and hitherto **unknown effect**

in terms of inhibiting blood supply to the tumor site and inducing tumor cell lysis is achieved simultaneously.”

Applicant’s response to the 35 USC 103 (a) rejection of claims 1 and 3:

Applicant respectfully disagrees that claim 1 is rendered obvious by a combination of Yanai and Kokura. The amended claim 1 now presented recites a salt solution mixture of a polyunsaturated fatty acid in the form of a salt solution....., which is not taught by either Yanai or Kokura. The salt solution could comprise either lithium or sodium or potassium, or any other suitable salt as supported by the text as originally filed.

Anti-angiogenic substances such as Angiostatin and Endostatin are proteins made by the body, and if made outside, are unstable and deficient (vide: first paragraph of text page 18 as originally filed). Applicant has discovered that these proteins can be stabilized and potentiated by mixing them with a suitable polyunsaturated fatty acid and administering the mixture in a salt solution, e.g., Lithium salt solution.

Neither of the references Yanai or Kokura has any teaching, nor suggestion justifying a combination of a fatty acid and an anti-angiogenic substance. The references teach administering an anti-angiogenic substance or a fatty acid separately and independently and have no suggestion that their single and separate use is deficient and they need to be combined. It is submitted that the examiner’s suggestion that the two references could be combined, is in hindsight. In re Piasecki, 223 USPQ 785 (CAFC 1984) seems to be on point.

For an obviousness rejection to apply over a combination of references, the prior art must suggest the desirability of the combination, and neither of the two references Yanai and Kokura suggests such desirability for combination. ACS Hospital Systems, Inc v. Montefiore Hospital, 221 U.S.P.Q. 929 (CAFC 1984), and also In re Fine, 5 USPQ 2d 1596 (CAFC 1988) seem to be on point.

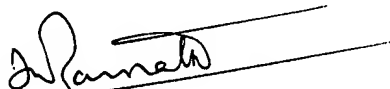
Applicant as a medical practitioner and a researcher has discovered and found that unexpected results in terms of **total blood flow stoppage** and necrosis in the tumor region are obtained by the method of administering a salt solution mixture of an anti-angiogenic substance along with a selected fatty acid. Such method is presently recited in the amended claim1. Applicant would be happy to submit a 37 CFR 1.132 affidavit in support of his unexpected finding, if so directed by the USPTO.

In view of the foregoing considerations, Applicant believes that the obviousness rejection of claims 1 and 3, based on a combination of Yanai and Kokura is not applicable and should be rescinded. Claim 3 is now amended to recite "lithium salt solution". Claims 4 and 5 are unamended. Only a minor amendment in claim 6 is made in terminology. Claim 7 is amended to delete "co-valently linked" in favor the term "coupled", and additionally to clarify certain terminology. A favorable consideration of the amended claims 1, 3, 6 and 7, and an indication of allowance of all the claims is earnestly requested. It is believed that no fees are due at this time.

**It is requested that the only figure (figure 1) in the present application be transferred to the new text of the substitute specification from the existing application on file**

If a brief telephone discussion of outstanding issues would expedite prosecution, the Examiner is requested to call the undersigned at **215 661 1140** during office hours.

Respectfully submitted,

  
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December 19, 2005

